Complete Summary

GUIDELINE TITLE

Early and locally advanced breast cancer. Diagnosis and treatment.

BIBLIOGRAPHIC SOURCE(S)

National Collaborating Centre for Cancer. Early and locally advanced breast cancer: diagnosis and treatment. London (UK): National Institute for Health and Clinical Excellence (NICE); 2009 Feb. 37 p. (NICE clinical guideline; no. 80).

GUIDELINE STATUS

This is the current release of the guideline.

This guideline updates previous versions: National Institute for Health and Clinical Excellence (NICE). Trastuzumab for the adjuvant treatment of early-stage HER2-positive breast cancer. London (UK): National Institute for Health and Clinical Excellence (NICE); 2006 Aug. 23 p. (Technology appraisal guidance; no. 107).

National Institute for Health and Clinical Excellence (NICE). Paclitaxel for the adjuvant treatment of early node-positive breast cancer. London (UK): National Institute for Health and Clinical Excellence (NICE); 2006 Sep. 18 p. (Technology appraisal guidance; no. 108).

National Institute for Health and Clinical Excellence (NICE). Docetaxel for the adjuvant treatment of early node-positive breast cancer. London (UK): National Institute for Health and Clinical Excellence (NICE); 2006 Sep. 21 p. (Technology appraisal guidance; no. 109).

**** REGULATORY ALERT ****

FDA WARNING/REGULATORY ALERT

Note from the National Guideline Clearinghouse: This guideline references a drug(s) for which important revised regulatory and/or warning information has been released.

- December 16, 2008 - Antiepileptic drugs: The U.S. Food and Drug Administration (FDA) has completed its analysis of reports of suicidality (suicidal behavior or ideation [thoughts]) from placebo-controlled clinical trials of drugs used to treat epilepsy, psychiatric disorders, and other conditions. Based on the outcome of this review, FDA is requiring that all manufacturers of drugs in this class include a Warning in their labeling and develop a Medication Guide to be provided to patients prescribed these drugs

to inform them of the risks of suicidal thoughts or actions. FDA expects that the increased risk of suicidality is shared by all antiepileptic drugs and anticipates that the class labeling change will be applied broadly.

COMPLETE SUMMARY CONTENT

SCOPE

DISEASE/CONDITION(S)

Early and locally advanced breast cancer

GUIDELINE CATEGORY

Counseling
Diagnosis
Evaluation
Management
Treatment

CLINICAL SPECIALTY

Family Practice
Internal Medicine
Obstetrics and Gynecology
Oncology
Pathology
Radiation Oncology
Surgery

INTENDED USERS

Advanced Practice Nurses
Health Care Providers
Nurses
Patients
Pharmacists

Physician Assistants
Physicians

GUIDELINE OBJECTIVE(S)

To offer best practice advice on the care of patients with early or locally advanced breast cancer

TARGET POPULATION

- Women with newly diagnosed invasive adenocarcinoma of the breast of clinical stages 1 and 2. This is where the primary tumour is less than 5 cm in maximum diameter and there is no sign of spread beyond the breast and axillary lymph nodes.
- Women with invasive adenocarcinoma of the breast of clinical stage 3. This includes primary tumours which may be larger than 5 cm in diameter (and includes inflammatory carcinoma).
- Men with newly diagnosed invasive adenocarcinoma of the breast of clinical stages 1, 2 and 3
- Women with newly diagnosed ductal carcinoma in situ
- Women with Paget's disease of the breast

Note: This guideline does not cover:

- Women and men with invasive adenocarcinoma of the breast of clinical stage 4. Refer to the National Guideline Clearinghouse (NGC) summary of the National Institute for Health and Clinical Excellence (NICE) clinical guideline; no 81. Advanced breast cancer: diagnosis and treatment.
- Women and men with rare breast tumours (for example, angiosarcoma, lymphoma)
- Women and men with benign breast tumours (for example, fibroadenoma, phyllodes tumour)
- Women with lobular carcinoma in situ
- Women with an increased risk of breast cancer due to family history. This population is covered by Familial breast cancer (NICE clinical guideline no. 14 [2004]).

INTERVENTIONS AND PRACTICES CONSIDERED

Diagnosis/Evaluation

1. Diagnostic investigation by triple assessment (clinical assessment, mammography and/or ultrasound)
2. Preoperative assessment of the breast and axilla
3. Magnetic resonance imaging as needed
4. Preoperative staging of the axilla using ultrasound and ultrasound-guided needle sampling
5. Sentinel lymph node biopsy
6. Pathological investigation including estrogen receptor and human epidermal growth receptor 2 (HER2) analysis

Management/Treatment

1. Surgical management, including plastic surgery for breast reconstruction
2. Entering patients with ductal carcinoma in situ into the Sloane Project
3. Providing patients with information and support

4. Adjuvant therapy planning
5. Endocrine therapy
    - Ovarian suppression/ablation
    - Tamoxifen
    - Aromatase inhibitors (anastrozole, letrozole, exemestane)
6. Chemotherapy
    - Docetaxel
7. Biological therapy
    - Trastuzumab
    - Monitoring cardiac function before and during trastuzumab therapy
8. Radiotherapy
    - Adjuvant radiotherapy
    - External beam radiotherapy
9. Assessment and treatment of bone loss
    - Dual x-ray absorptiometry scan
    - Bisphosphonates therapy
10. Management of complications and menopausal symptoms
    - Management of lymphedema
    - Physiotherapy for arm mobility
    - Discontinuation of hormone replacement therapy
    - Selective serotonin reuptake inhibitor antidepressants
    - Clonidine, venlafaxine, gabapentin for hot flushes
11. Follow-up imaging
12. Clinical follow-up

MAJOR OUTCOMES CONSIDERED

- Clinical effectiveness
    - Overall and disease-free survival
    - Cancer recurrence
    - Metastases
    - Adverse events
- Cost-effectiveness

METHODOLOGY

METHODS USED TO COLLECT/SELECT EVIDENCE

Searches of Electronic Databases

DESCRIPTION OF METHODS USED TO COLLECT/SELECT THE EVIDENCE

Note from the National Guideline Clearinghouse (NGC): This guideline was developed by the National Collaborating Centre for Cancer (NCC-C) on behalf of the National Institute for Health and Clinical Excellence (NICE). See the "Availability of Companion Documents" field for the full version of this guidance.

Review of Clinical Literature

At the beginning of the development phase, initial scoping searches were carried out to identify any relevant guidelines (local, national or international) produced

by other groups or institutions. Additionally, stakeholder organisations were invited to submit evidence for consideration by the guideline development group (GDG), provided it was relevant to the agreed list of clinical questions.

In order to answer each question the NCC-C information specialist developed a search strategy to identify relevant published evidence for both clinical and cost effectiveness. Key words and terms for the search were agreed in collaboration with the GDG. When required, the health economist searched for supplementary papers to inform detailed health economic work, for example modelling (see section on 'Incorporating Health Economic Evidence' below).

Papers that were published or accepted for publication in peer-reviewed journals were considered as evidence. Search filters, such as those to identify systematic reviews (SRs) and randomized controlled trials (RCTs) were applied to the search strategies when there was a wealth of these types of studies. No language restrictions were applied to the search; however, foreign language papers were not requested or reviewed (unless of particular importance to that question).

The following databases were included in the literature search:

- The Cochrane Library
- Medline and Premedline 1950 onwards
- Excerpta Medica (Embase) 1980 onwards
- Cumulative Index to Nursing and Allied Health Literature (Cinahl) 1982 onwards
- Allied & Complementary Medicine (AMED) 1985 onwards
- British Nursing Index (BNI) 1994 onwards
- Psychinfo 1806 onwards
- Web of Science 1970 onwards. [specifically Science Citation Index Expanded (SCI-EXPANDED) and Social Sciences Citation Index (SSCI)]
- System for Information on Grey Literature In Europe (SIGLE) 1980–2005
- Biomed Central 1997 onwards
- National Research Register (NRR)
- Current Controlled Trials

From this list the information specialist sifted and removed any irrelevant material based on the title or abstract before passing to the researcher. All the remaining articles were then stored in a Reference Manager electronic library.

Searches were updated and re-run 6–8 weeks before the stakeholder consultation, thereby ensuring that the latest relevant published evidence was included in the database. Any evidence published after this date was not included. For the purposes of updating this guideline, July 2008 should be considered the starting point for searching for new evidence.

Further details of the search strategies, including the methodological filters used, are provided in the evidence review (and appear on the accompanying CD-ROM to this guideline).

Incorporating Health Economics Evidence

The aim of the economic input into the guideline was to inform the GDG of potential economic issues relating to early breast cancer. It is important to investigate whether health services are both clinically effective and cost effective, i.e. are they 'value for money'. The health economist helped the GDG by identifying priority topics within the guideline that might benefit from economic analysis, reviewing the available economic evidence and, where necessary, conducting economic analysis. Where published economic evaluation studies were identified that addressed the economic issues for a clinical question, these are presented alongside the clinical evidence wherever possible.

In order to assess the cost effectiveness of each priority topic, a comprehensive systematic review of the economic literature was conducted. For those clinical areas reviewed, the information specialists used a similar search strategy as used for the review of clinical evidence but with the inclusion of a health economics and quality of life filter.

Each search strategy was designed to find any applied study estimating the cost or cost effectiveness of the topic under consideration. A health economist reviewed abstracts and relevant papers were ordered for appraisal.

Published economic evidence was obtained from a variety of sources:

- Medline 1966 onwards
- Embase 1980 onwards
- NHS Economic Evaluations Database (NHS EED)
- EconLit 1969 onwards

NUMBER OF SOURCE DOCUMENTS

Not stated

METHODS USED TO ASSESS THE QUALITY AND STRENGTH OF THE EVIDENCE

Weighting According to a Rating Scheme (Scheme Given)

RATING SCHEME FOR THE STRENGTH OF THE EVIDENCE

Levels of Evidence for Intervention Studies

Level	Source of Evidence
1++	High-quality meta-analyses, systematic reviews of randomised controlled trials (RCTs), or RCTs with a very low risk of bias.
1+	Well-conducted meta-analyses, systematic reviews of RCTs, or RCTs with a low risk of bias.
1–	Meta-analyses, systematic reviews of RCTs, or RCTs with a high risk of bias.
2++	High-quality systematic reviews of case-control or cohort studies.

Level	Source of Evidence
	High-quality case-control or cohort studies with a very low risk of confounding or bias and a high probability that the relationship is causal.
2+	Well-conducted case-control or cohort studies with a low risk of confounding, bias or chance and a moderate probability that the relationship is causal.
2–	Case-control or cohort studies with a high risk of confounding, bias or chance and a significant risk that the relationship is not causal.
3	Non-analytic studies (for example case reports, case series).
4	Expert opinion, formal consensus.

METHODS USED TO ANALYZE THE EVIDENCE

Review of Published Meta-Analyses
Systematic Review with Evidence Tables

DESCRIPTION OF THE METHODS USED TO ANALYZE THE EVIDENCE

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Critical Appraisal and Evidence Grading

Following the literature search one researcher independently scanned the titles and abstracts of every article for each question, and full publications were obtained for any studies considered relevant or where there was insufficient information from the title and abstract to make a decision.

The researcher then individually applied the inclusion/exclusion criteria to determine which studies would be relevant for inclusion and subsequent appraisal. Lists of excluded papers were generated for each question and the rationale for the exclusion was presented to the Guideline Development Group (GDG) when required.

The researcher then critically appraised the full papers. Critical appraisal checklists were compiled for each paper and one researcher undertook the critical appraisal and data extraction.

The researcher assessed the quality of eligible studies by referring to the Scottish Intercollegiate Guidelines Network (SIGN) criteria for systematic reviews/meta-analyses and randomised control trials (see "Rating Scheme for the Strength of the Evidence" above). Evidence relating to clinical effectiveness was classified using this established hierarchical system. However this checklist is less appropriate for studies reporting diagnostic tests of accuracy. In the absence of a validated hierarchy for this type of test, NICE suggests levels of evidence that take into account the factors likely to affect the validity of these studies.

For all the relevant appraised studies for a particular question, data on the type of population, intervention, comparator and outcomes (PICO) was recorded in evidence tables and an accompanying evidence summary prepared for the GDG (see evidence review [see "Availability of Companion Documents" field]). All the evidence was considered carefully by the GDG for accuracy and completeness.

All procedures were fully compliant with NICE methodology as detailed in the 'NICE guidelines manual'. In general, no formal contact was made with authors; however, there were ad hoc occasions when this was required in order to clarify specific details.

METHODS USED TO FORMULATE THE RECOMMENDATIONS

Expert Consensus

DESCRIPTION OF METHODS USED TO FORMULATE THE RECOMMENDATIONS

Note from the National Guideline Clearinghouse (NGC): This guideline was developed by the National Collaborating Centre for Cancer (NCC-C) on behalf of the National Institute for Health and Clinical Excellence (NICE). See the "Availability of Companion Documents" field for the full version of this guidance.

The Guideline Development Group (GDG)

The Early Breast Cancer GDG was recruited in line with the existing NICE protocol as set out in the 'NICE guidelines manual'. The first step was to appoint a Chair and a Lead Clinician. Advertisements were placed for both posts and candidates were informally interviewed prior to being offered the role. The NCC-C Director, GDG Chair and Lead Clinician identified a list of specialties that needed to be represented on the GDG. Requests for nominations were sent to the main stakeholder organisations and patient organisations/charities (see Appendix 8.2 of the full version of the original guideline document). Individual GDG members were selected by the NCC-C Director, GDG Chair and Lead Clinician, based on their application forms, following nomination from their respective stakeholder organisation. The guideline development process was supported by staff from the NCC-C, who undertook the clinical and health economics literature searches, reviewed and presented the evidence to the GDG, managed the process and contributed to drafting the guideline.

Guideline Development Group Meetings

Fifteen GDG meetings were held between 10-11 April 2006 and 19-20 June 2008. During each GDG meeting (either held over one or two days) clinical questions and clinical and economic evidence were reviewed, assessed and recommendations formulated. At each meeting patient/carer and service-user concerns were routinely discussed as part of a standing agenda item.

NCC-C project managers divided the GDG workload by allocating specific clinical questions, relevant to their area of clinical practice, to small sub-groups of the GDG in order to simplify and speed up the guideline development process. These

groups considered the evidence, as reviewed by the researcher, and synthesised it into draft recommendations prior to presenting it to the GDG as a whole. Each clinical question was led by a GDG member with expert knowledge of the clinical area (usually one of the healthcare professionals). The GDG subgroups often helped refine the clinical questions and the clinical definitions of treatments. They also assisted the NCC-C team in drafting the section of the guideline relevant to their specific topic.

Patient/Carer Members

Individuals with direct experience of early breast cancer services gave an integral user focus to the GDG and the guideline development process. The GDG included three patient/carer members. They contributed as full GDG members to writing the clinical questions, helping to ensure that the evidence addressed their views and preferences, highlighting sensitive issues and terminology relevant to the guideline and bringing service-user research to the attention of the GDG.

Developing Clinical Evidence-Based Questions

An extensive list of potential topics for the guideline to investigate was compiled by the NCC-C Director and guideline development group (GDG) Chair and Lead Clinician in consultation with a small number of breast cancer multidisciplinary teams across England and Wales. Refer to the "Methodology" section of the full version of the original guideline document for the methods used in developing these questions.

The final list of clinical questions can be found in Appendix 7 of the full version of the original guideline document.

Linking to NICE Technology Appraisals

When this guideline was commissioned there were several published technology appraisals (TAs) and some TAs in development which were relevant to the guideline. Two methodological approaches were taken to link to these pieces of guidance.

1. Technology appraisals in development

   Once the TA had been published, its recommendations were reproduced unchanged in the most appropriate section of the guideline. To ensure accurate exchange of information between the GDG and the appraisals team, a representative from the GDG attended all Appraisal Committee meetings.

2. Published technology appraisals

   Published TAs are periodically reviewed to determine if they need to be updated. If the decision was taken by NICE, after consultation with stakeholders, that a TA should be updated within this guideline the GDG determined whether any new evidence had become available since the publication of the appraisal which meant the original recommendations needed to be changed. Changes to recommendations needed to be supported

by cost-effectiveness analysis. Those TAs which were updated into this guideline were subject to the same methodology as all other clinical questions.

For published TAs which were not due for review during the development of this guideline, their recommendations were reproduced unchanged in the most appropriate section.

Agreeing the Recommendations

For each clinical question the GDG were presented with a summary of the clinical evidence, and where appropriate economic evidence, derived from the studies reviewed and appraised. From this information the GDG were able to derive the guideline recommendations. The link between the evidence and the view of the GDG in making each recommendation is made explicit in the accompanying qualifying statement.

Qualifying Statements

As clinical guidelines are currently formatted, there is limited scope for expressing how and why a GDG made a particular recommendation from the evidence of clinical and cost effectiveness.

To make this process more transparent to the reader, the NCC-C felt the need for an explicit, easily understood and consistent way of expressing the reasons for making each recommendation.

The way they have chosen to do this is by writing a 'qualifying statement' to accompany every recommendation and will usually cover:

- The strength of evidence about benefits and harms for the intervention being considered
- The degree of consensus within the GDG
- The costs and cost effectiveness (if formally assessed by the health economics team)

Where evidence was weak or lacking the GDG agreed the final recommendations through informal consensus. Shortly before the consultation period, ten key priorities and five key research recommendations were selected by the GDG for implementation and the patient algorithm were agreed. To avoid giving the impression that higher grade recommendations are of higher priority for implementation, NICE no longer assigns grades to recommendations.

RATING SCHEME FOR THE STRENGTH OF THE RECOMMENDATIONS

Not applicable

COST ANALYSIS

Economic Modelling

In addition to the review of the relevant clinical evidence, the guideline development group (GDG) were required to determine whether or not the cost effectiveness of each of the individual clinical questions should be investigated. After the clinical questions were decided, the GDG agreed which topics were an 'economic priority' for modelling. These 'economic priorities' were chosen on the basis of the following criteria, in broad accordance with the 'NICE guidelines manual:

Overall Relevance of the Topic

- *The number of patients affected*: interventions affecting relatively large numbers of patients were given a higher economic priority than those affecting fewer patients
- *The health benefits to the patient*: interventions that that were considered to have a potentially significant impact on both survival and quality of life were given a higher economic priority
- *The per patient cost*: interventions with potentially high financial (cost/savings) implications were given high priority compared to interventions expected to have lower financial implications
- *Likelihood of changing clinical practice*: priority was given to topics that were considered likely to represent a significant change to existing clinical practice

Uncertainty

- *High level of existing uncertainty*: higher economic priority was given to clinical questions in which further economic analysis was considered likely to reduce current uncertainty over cost effectiveness. Low priority was given to clinical questions when the current literature implied a clearly 'attractive' or 'unattractive' incremental cost effectiveness ratio, which was regarded as generalisable to a UK healthcare setting
- *Likelihood of reducing uncertainty with further analyses (feasibility issues)*: when there was poor evidence for the clinical effectiveness of an intervention, then there was considered to be less justification for an economic analysis to be undertaken

Once the economic priority clinical questions had been chosen, the next task was to perform a systematic review of the cost effectiveness literature. When relevant published evidence was identified and considered to be of sufficient quality, this information was used to inform the recommendation for that specific clinical question. When no relevant cost effectiveness evidence was identified, or when it was not considered to be of reasonable quality, consideration was given to building a de novo economic model. This decision was made by the GDG based on an assessment of the available evidence required to populate a potential economic model.

For those clinical questions where an economic model was required, the information specialist performed supplemental literature searches to obtain additional data for modelling. Assumptions and designs of the models were explained to and agreed by the GDG members during meetings, and they commented on subsequent revisions.

The clinical question in this guideline selected for modelling was chosen because at the time it was considered likely that the recommendations under consideration could substantially change clinical practice in the NHS and have important consequences for resource use. The details of the model are presented in the evidence review and Appendix 3 in the full version of the original guideline document. During the modeling process the following general principles were adhered to:

- The GDG Chair and Clinical Lead were consulted during the construction and interpretation of the model
- The model was based on the best evidence from the systematic review
- Model assumptions were reported fully and transparently
- The results were subject to thorough sensitivity analysis and limitations discussed costs were calculated from a health services perspective

A costing report also accompanies the clinical guideline: 'Early and Locally Advance Breast Cancer: Costing Report' is available online at www.nice.org.uk.

METHOD OF GUIDELINE VALIDATION

External Peer Review
Internal Peer Review

DESCRIPTION OF METHOD OF GUIDELINE VALIDATION

The draft of the guideline was prepared by National Collaborating Centre for Cancer (NCC-C) staff in partnership with the Guideline Development Group (GDG) Chair and Lead Clinician. This was then discussed and agreed with the GDG and subsequently forwarded to the National Institute for Health and Clinical Excellence (NICE) for consultation with stakeholders.

RECOMMENDATIONS

MAJOR RECOMMENDATIONS

Note from the National Guideline Clearinghouse (NGC): This guideline was developed by the National Collaborating Centre for Cancer (NCC-C) on behalf of the National Institute for Health and Clinical Excellence (NICE). See the "Availability of Companion Documents" field for the full version of this guidance.

Referral, Diagnosis and Preoperative Assessment

Patients with symptoms that could be caused by breast cancer are referred by their general practitioner (GP) to designated breast clinics in local hospitals (see NICE clinical guideline 27, 'Referral guidelines for suspected cancer'; www.nice.org.uk/CG27). In addition, women aged between 50 and 70 are invited for screening mammography every 3 years through the National Health Service Breast Screening Programme (NHSBSP) in England or the Breast Test Wales Screening Programme (BTWSP) in Wales. For most patients, whether they are referred following breast screening or after presentation to a GP, diagnosis in the breast clinic is made by triple assessment (clinical assessment, mammography

and/or ultrasound imaging, and core biopsy and/or fine needle aspiration cytology). It is best practice to carry out these assessments at the same visit (see National Institute for Health and Clinical Excellence (NICE) cancer service guidance 'Improving outcomes in breast cancer – Manual update'; www.nice.org.uk/csgbc).

Preoperative Assessment of the Breast and Axilla

- The routine use of magnetic resonance imaging (MRI) of the breast is not recommended in the preoperative assessment of patients with biopsy-proven invasive breast cancer or ductal carcinoma in situ (DCIS).
- Offer MRI of the breast to patients with invasive breast cancer:
    - If there is discrepancy regarding the extent of disease from clinical examination, mammography and ultrasound assessment for planning treatment
    - If breast density precludes accurate mammographic assessment
    - To assess the tumour size if breast conserving surgery is being considered for invasive lobular cancer

Preoperative Staging of the Axilla

- Pretreatment ultrasound evaluation of the axilla should be performed for all patients being investigated for early invasive breast cancer, and, if morphologically abnormal lymph nodes are identified, ultrasound-guided needle sampling should be offered.

Providing Information and Psychological Support

- All members of the breast cancer clinical team should have completed an accredited communication skills training programme.
- All patients with breast cancer should be assigned to a named breast care nurse specialist who will support them throughout diagnosis, treatment and follow-up.
- All patients with breast cancer should be offered prompt access to specialist psychological support and, where appropriate, psychiatric services.

Surgery to the Breast

Ductal Carcinoma In Situ

- For all patients treated with breast conserving surgery for DCIS a minimum of 2 mm radial margin of excision is recommended with pathological examination to NHSBSP reporting standards. Re-excision should be considered if the margin is less than 2 mm, after discussion of the risks and benefits with the patient.
- Enter patients with screen-detected DCIS into the Sloane Project (UK DCIS audit) (www.sloaneproject.co.uk).
- All breast units should audit their recurrence rates after treatment for DCIS.

Paget's Disease

- Offer breast conserving surgery with removal of the nipple-areolar complex as an alternative to mastectomy for patients with Paget's disease of the nipple that has been assessed as localised. Offer oncoplastic repair techniques to maximise cosmesis.

Surgery to the Axilla

Invasive Breast Cancer

Minimal surgery, rather than lymph node clearance, should be performed to stage the axilla for patients with early invasive breast cancer and no evidence of lymph node involvement on ultrasound or a negative ultrasound-guided needle biopsy. Sentinel lymph node biopsy (SLNB) is the preferred technique.

- SLNB should only be performed by a team that is validated in the use of the technique, as identified in the New Start training programme.[1]
- Perform SLNB using the dual technique with isotope and blue dye.
- Breast units should audit their axillary recurrence rates.

Ductal Carcinoma In Situ

- Do not perform SLNB routinely in patients with a preoperative diagnosis of DCIS who are having breast conserving surgery, unless they are considered to be at a high risk of invasive disease.[2]
- Offer SLNB to all patients who are having a mastectomy for DCIS.

[1] NEW START Sentinel Lymph Node Biopsy Training Programme, The Royal College of Surgeons of England (www.rcseng.ac.uk/education/courses/new_start.html).

[2] Patients considered at high risk of invasive disease include those with a palpable mass or extensive microcalcifications.

Evaluation and Management of a Positive Sentinel Lymph Node

- Offer further axillary treatment to patients with early invasive breast cancer who:
    - Have macrometastases or micrometastases shown in a sentinel lymph node
    - Have a preoperative ultrasound-guided needle biopsy with histologically proven metastatic cancer
- The preferred technique is axillary lymph node dissection (ALND) because it gives additional staging information.
- Do not offer further axillary treatment to patients found to have only isolated tumour cells in their sentinel lymph nodes. These patients should be regarded as lymph node-negative.

Breast Reconstruction

- Discuss immediate breast reconstruction with all patients who are being advised to have a mastectomy, and offer it except where significant comorbidity or (the need for) adjuvant therapy may preclude this option. All

appropriate breast reconstruction options should be offered and discussed with patients, irrespective of whether they are all available locally.

Postoperative Assessment and Adjuvant Therapy Planning

Predictive Factors

- Assess oestrogen receptor (ER) status of all invasive breast cancers, using immunohistochemistry with a standardised and qualitatively assured methodology, and report the results quantitatively.
- Do not routinely assess progesterone receptor status of tumours in patients with invasive breast cancer.
- Test human epidermal growth receptor 2 (HER2) status of all invasive breast cancers, using a standardised and qualitatively assured methodology.
- Ensure that the results of ER and HER2 assessments are available and recorded at the multidisciplinary team meeting when guidance about systemic treatment is made.

Adjuvant Therapy Planning

- Consider adjuvant therapy for all patients with early invasive breast cancer after surgery at the multidisciplinary team meeting and ensure that decisions are recorded.
- Decisions about adjuvant therapy should be made based on assessment of the prognostic and predictive factors, the potential benefits and side effects of the treatment. Decisions should be made following discussion of these factors with the patient.
- Consider using Adjuvant! Online (www.adjuvantonline.com) to support estimations of individual prognosis and the absolute benefit of adjuvant treatment for patients with early invasive breast cancer.
- Start adjuvant chemotherapy or radiotherapy as soon as clinically possible within 31 days of completion of surgery[3] in patients with early breast cancer having these treatments.

[3] Department of Health (2007) Cancer reform strategy. London: Department of Health. (At present no equivalent target has been set by the Welsh Assembly Government.

Endocrine Therapy

Ovarian Suppression/Ablation for Early Invasive Breast Cancer

- Do not offer adjuvant ovarian ablation/suppression to premenopausal women with ER-positive early invasive breast cancer who are being treated with tamoxifen and, if indicated, chemotherapy.
- Offer adjuvant ovarian ablation/suppression in addition to tamoxifen to premenopausal women with ER-positive early invasive breast cancer who have been offered chemotherapy but have chosen not to have it.

Aromatase Inhibitors for Early Invasive Breast Cancer

- Postmenopausal women with ER-positive early invasive breast cancer who are not considered to be at low risk[4] should be offered an aromatase inhibitor,

either anastrozole or letrozole, as their initial adjuvant therapy. Offer tamoxifen if an aromatase inhibitor is not tolerated or contraindicated.

- Offer an aromatase inhibitor, either exemestane or anastrozole, instead of tamoxifen to postmenopausal women with ER-positive early invasive breast cancer who are not low risk[4] and who have been treated with tamoxifen for 2–3 years.
- Offer additional treatment with the aromatase inhibitor letrozole for 2–3 years to postmenopausal women with lymph node-positive ER-positive early invasive breast cancer who have been treated with tamoxifen for 5 years.
- The aromatase inhibitors anastrozole, exemestane and letrozole, within their licensed indications, are recommended as options for the adjuvant treatment of early ER-positive invasive breast cancer in postmenopausal women[5].
- The choice of treatment should be made after discussion between the responsible clinician and the woman about the risks and benefits of each option. Factors to consider when making the choice include whether the woman has received tamoxifen before, the licensed indications and side-effect profiles of the individual drugs and, in particular, the assessed risk of recurrence.[5]

[4] Low-risk patients are those in the EPG or GPG (excellent prognostic group or good prognostic group) in the Nottingham Prognostic Index (NPI), who have 10-year predictive survivals of 96% and 93%, respectively. They would have a similar prediction using Adjuvant! Online.

[5] This recommendation is from Hormonal therapies for the adjuvant treatment of early oestrogen-receptor-positive breast cancer (NICE technology appraisal guidance 112).

Tamoxifen for Ductal Carcinoma In Situ

- Do not offer adjuvant tamoxifen after breast conserving surgery to patients with DCIS.

Chemotherapy

- Offer docetaxel to patients with lymph node-positive breast cancer as part of an adjuvant chemotherapy regimen.
- Do not offer paclitaxel as an adjuvant treatment for lymph node-positive breast cancer.

Biological Therapy

- Offer trastuzumab, given at 3-week intervals for 1 year or until disease recurrence (whichever is the shorter period), as an adjuvant treatment to women with HER2-positive early invasive breast cancer following surgery, chemotherapy, and radiotherapy when applicable.
- Assess cardiac function before starting treatment with trastuzumab. Do not offer trastuzumab treatment to women who have any of the following:
    - A left ventricular ejection fraction (LVEF) of 55% or less
    - A history of documented congestive heart failure
    - High-risk uncontrolled arrhythmias
    - Angina pectoris requiring medication
    - Clinically significant valvular disease
    - Evidence of transmural infarction on electrocardiograph (ECG)
    - Poorly controlled hypertension

- Repeat cardiac functional assessments every 3 months during trastuzumab treatment. If the LVEF drops by 10 percentage (ejection) points or more from baseline and to below 50%, then trastuzumab treatment should be suspended. Restart trastuzumab therapy only after further cardiac assessment and a fully informed discussion of the risks and benefits with the woman.

Assessment and Treatment of Bone Loss

- Patients with early invasive breast cancer should have a baseline dual energy X-ray absorptiometry (DEXA) scan to assess bone mineral density if they:
    - Are starting adjuvant aromatase inhibitor treatment
    - Have treatment-induced menopause
    - Are starting ovarian ablation/suppression therapy
- Do not offer a DEXA scan to patients with early invasive breast cancer who are receiving tamoxifen alone, regardless of pretreatment menopausal status.
- Offer bisphosphonates to patients identified by algorithms 1 and 2 in 'Guidance for the management of breast cancer treatment-induced bone loss: a consensus position statement from a UK expert group' (2008). (see appendix 2 in the full guideline document, available from www.nice.org.uk/CG80FullGuideline).

Radiotherapy

Radiotherapy after Breast Conserving Surgery

- Patients with early invasive breast cancer who have had breast conserving surgery with clear margins should have breast radiotherapy.
- Offer adjuvant radiotherapy to patients with DCIS following adequate breast conserving surgery and discuss with them the potential benefits and risks (see recommendation under "Surgery to the Breast, Ductal Carcinoma in Situ" above).

Radiotherapy after Mastectomy

- Offer adjuvant chest wall radiotherapy to patients with early invasive breast cancer who have had a mastectomy and are at a high risk of local recurrence. Patients at a high risk of local recurrence include those with four or more positive axillary lymph nodes or involved resection margins.
- Consider entering patients who have had a mastectomy for early invasive breast cancer and who are at an intermediate risk of local recurrence into the current UK trial (SUPREMO) assessing the value of postoperative radiotherapy. Patients at an intermediate risk of local recurrence include those with one to three lymph nodes involved, lymphovascular invasion, histological grade 3 tumours, ER-negative tumours, and those aged under 40.
- Do not offer radiotherapy following mastectomy to patients with early invasive breast cancer who are at low risk of local recurrence (for example, most patients who are lymph node-negative).

Dose Fractionation

- Use external beam radiotherapy giving 40 Gy in 15 fractions as standard practice for patients with early invasive breast cancer after breast conserving surgery or mastectomy.

Breast Boost

- Offer an external beam boost to the site of local excision to patients with early invasive breast cancer and a high risk of local recurrence, following breast conserving surgery with clear margins and whole breast radiotherapy.
- If an external beam boost to the site of local excision following breast conserving surgery is being considered in patients with early invasive breast cancer, inform the patient of the side effects associated with this intervention, including poor cosmesis, particularly in women with larger breasts.

Radiotherapy to Nodal Areas

- Do not offer adjuvant radiotherapy to the axilla or supraclavicular fossa to patients with early breast cancer who have been shown to be histologically lymph node-negative.
- Do not offer adjuvant radiotherapy to the axilla after ALND for early breast cancer.
- If ALND is not possible following a positive axillary SLNB or four-node sample, offer adjuvant radiotherapy to the axilla to patients with early breast cancer (see recommendations under "Surgery to the Axilla" above).
- Offer adjuvant radiotherapy to the supraclavicular fossa to patients with early breast cancer and four or more involved axillary lymph nodes.
- Offer adjuvant radiotherapy to the supraclavicular fossa to patients with early breast cancer and one to three positive lymph nodes if they have other poor prognostic factors (for example, T3 and/or histological grade 3 tumours) and good performance status.
- Do not offer adjuvant radiotherapy to the internal mammary chain to patients with early breast cancer who have had breast surgery.

Primary Systemic Therapy

Early Breast Cancer

- Treat patients with early invasive breast cancer, irrespective of age, with surgery and appropriate systemic therapy, rather than endocrine therapy alone, unless significant comorbidity precludes surgery.
- Preoperative systemic therapy can be offered to patients with early invasive breast cancer who are considering breast conserving surgery that is not advisable at presentation. However, the increased risk of local recurrence with breast conserving surgery and radiotherapy rather than mastectomy after systemic therapy should be discussed with the patient.

Locally Advanced or Inflammatory Breast Cancer

- Offer local treatment by mastectomy (or, in exceptional cases, breast conserving surgery) followed by radiotherapy to patients with locally

advanced or inflammatory breast cancer who have been treated with chemotherapy.

Complications of Local Treatment and Menopausal Symptoms

Lymphoedema

- Inform all patients with early breast cancer about the risk of developing lymphoedema and give them relevant written information before treatment with surgery and radiotherapy.
- Give advice on how to prevent infection or trauma that may cause or exacerbate lymphoedema to patients treated for early breast cancer.
- Ensure that all patients with early breast cancer who develop lymphoedema have rapid access to a specialist lymphoedema service.

Arm Mobility

- All breast units should have written local guidelines agreed with the physiotherapy department for postoperative physiotherapy regimens.
- Identify breast cancer patients with pre-existing shoulder conditions preoperatively as this may inform further decisions on treatment.
- Give instructions on functional exercises, which should start the day after surgery, to all breast cancer patients undergoing axillary surgery. This should include relevant written information from a member of the breast or physiotherapy team.
- Refer patients to the physiotherapy department if they report a persistent reduction in arm and shoulder mobility after breast cancer treatment.

Menopausal Symptoms

- Discontinue hormone replacement therapy (HRT) in women who are diagnosed with breast cancer.
- Do not offer HRT (including oestrogen/progestogen combination) routinely to women with menopausal symptoms and a history of breast cancer. HRT [6] may, in exceptional cases, be offered to women with severe menopausal symptoms and with whom the associated risks have been discussed.
- Offer information and counselling for all women about the possibility of early menopause and menopausal symptoms associated with breast cancer treatment.
- Tibolone or progestogens are not recommended for women with menopausal symptoms who have breast cancer.

[6] The summaries of product characteristics state that HRT is contraindicated in women with known, past or suspected breast cancer. Informed consent should be obtained and documented.

- The selective serotonin re-uptake inhibitor antidepressants paroxetine[7] and fluoxetine[7] may be offered to women with breast cancer for relieving menopausal symptoms, particularly hot flushes, but not to those taking tamoxifen.
- Clonidine, venlafaxine[7] and gabapentin[7] should only be offered to treat hot flushes in women with breast cancer after they have been fully informed of the significant side effects.

- Soy (isoflavone), red clover, black cohosh, vitamin E and magnetic devices are not recommended for the treatment of menopausal symptoms in women with breast cancer.

[7] These drugs are not licensed for the stated use. Informed consent should be obtained and documented.

Follow-Up

Follow-Up Imaging

- Offer annual mammography to all patients with early breast cancer, including DCIS, until they enter the NHSBSP/BTWSP. Patients diagnosed with early breast cancer who are already eligible for screening should have annual mammography for 5 years.
- On reaching the NHSBSP/BTWSP screening age or after 5 years of annual mammography follow-up we recommend the NHSBSP/BTWSP stratify screening frequency in line with patient risk category.
- Do not offer mammography of the ipsilateral soft tissues after mastectomy.
- Do not offer ultrasound or MRI for routine post-treatment surveillance in patients who have been treated for early invasive breast cancer or DCIS.

Clinical Follow-Up

- After completion of adjuvant treatment (including chemotherapy, and/or radiotherapy where indicated) for early breast cancer, discuss with patients where they would like follow-up to be undertaken. They may choose to receive follow-up care in primary, secondary, or shared care.
- Patients treated for breast cancer should have an agreed, written care plan, which should be recorded by a named healthcare professional (or professionals), a copy sent to the GP and a personal copy given to the patient. This plan should include:
    - Designated named healthcare professionals
    - Dates for review of any adjuvant therapy
    - Details of surveillance mammography
    - Signs and symptoms to look for and seek advice on
    - Contact details for immediate referral to specialist care
    - Contact details for support services, for example support for patients with lymphoedema

CLINICAL ALGORITHM(S)

An algorithm for management of early and locally advanced breast cancer is provided in the full version of the original guideline document.

The following algorithms taken from 'Guidance for the management of breast cancer treatment-induced bone loss: A consensus position statement from a UK expert group" (2008) are provided in Appendix 2 of the full version of the original guideline:

- Women who experience premature menopause
- Post menopausal adjunctive treatment with aromatase inhibitors

EVIDENCE SUPPORTING THE RECOMMENDATIONS

TYPE OF EVIDENCE SUPPORTING THE RECOMMENDATIONS

The type of evidence supporting the recommendations is not specifically stated.

BENEFITS/HARMS OF IMPLEMENTING THE GUIDELINE RECOMMENDATIONS

POTENTIAL BENEFITS

Appropriate patient-centered diagnosis, treatment, and management of patients with early and locally advanced breast cancer

POTENTIAL HARMS

Adverse effects of chemotherapy, biological therapy, and radiotherapy, as well as surgical complications

CONTRAINDICATIONS

CONTRAINDICATIONS

Hormone replacement therapy is contraindicated in women with known, past or suspected breast cancer.

QUALIFYING STATEMENTS

QUALIFYING STATEMENTS

- This guidance represents the view of the National Institute for Health and Clinical Excellence (NICE), which was arrived at after careful consideration of the evidence available. Healthcare professionals are expected to take it fully into account when exercising their clinical judgement. However, the guidance does not override the individual responsibility of healthcare professionals to make decisions appropriate to the circumstances of the individual patient, in consultation with the patient and/or guardian or carer, and informed by the summary of product characteristics of any drugs they are considering.
- Implementation of this guidance is the responsibility of local commissioners and/or providers. Commissioners and providers are reminded that it is their responsibility to implement the guidance, in their local context, in light of their duties to avoid unlawful discrimination and to have regard to promoting equality of opportunity. Nothing in this guidance should be interpreted in a way that would be inconsistent with compliance with those duties.
- The Guideline Development Group assumes that healthcare professionals will use clinical judgment, knowledge and expertise when deciding whether it is appropriate to apply these guidelines. The recommendations cited here are a guide and may not be appropriate for use in all situations. The decision to adopt any of the recommendations cited here must be made by the

practitioner in light of individual patient circumstances, the wishes of the patient and clinical expertise.

- The National Collaborating Centre for Cancer disclaims any responsibility for damages arising out of the use or non-use of these guidelines and the literature used in support of these guidelines.
- While every effort has been made to ensure the accuracy of the information contained within this publication, the publisher can give no guarantee for information about drug dosage and application thereof contained in this book. In every individual case the respective user must check current indications and accuracy by consulting other pharmaceutical literature and following the guidelines laid down by the manufacturers of specific products and the relevant authorities in the country in which they are practising.
- This guideline does not include recommendations covering every detail of the diagnosis and treatment of early breast cancer. Instead the guideline developers have tried to focus on those areas of clinical practice that are (i) known to be controversial or uncertain; (ii) where there is identifiable practice variation; (iii) where there is a lack of high-quality evidence; or (iv) where NICE guidelines are likely to have most impact. More detail on how this was achieved is presented in the section on 'Developing Clinical Evidence Based Questions' in the original guideline document.

IMPLEMENTATION OF THE GUIDELINE

DESCRIPTION OF IMPLEMENTATION STRATEGY

The Healthcare Commission assesses the performance of National Health Service (NHS) organisations in meeting core and developmental standards set by the Department of Health in 'Standards for better health' (available from www.dh.gov.uk). Implementation of clinical guidelines forms part of the developmental standard D2. Core standard C5 says that national agreed guidance should be taken into account when NHS organisations are planning and delivering care.

NICE has developed tools to help organisations implement this guidance (listed below). These are available on our website (http://guidance.nice.org.uk/CG80).

- Slides highlighting key messages for local discussion
- Costing tools
    - Costing report to estimate the national savings and costs associated with implementation
    - Costing template to estimate the local costs and savings involved
- Audit support for monitoring local practice

Key Priorities for Implementation

Preoperative Assessment of the Breast

- Offer magnetic resonance imaging (MRI) of the breast to patients with invasive breast cancer:

- If there is discrepancy regarding the extent of disease from clinical examination, mammography and ultrasound assessment for planning treatment
- If breast density precludes accurate mammographic assessment
- To assess the tumour size if breast conserving surgery is being considered for invasive lobular cancer

Staging of the Axilla

- Pretreatment ultrasound evaluation of the axilla should be performed for all patients being investigated for early invasive breast cancer and, if morphologically abnormal lymph nodes are identified, ultrasound-guided needle sampling should be offered.

Surgery to the Axilla

- Minimal surgery, rather than lymph node clearance, should be performed to stage the axilla for patients with early invasive breast cancer and no evidence of lymph node involvement on ultrasound or a negative ultrasound-guided needle biopsy. Sentinel lymph node biopsy (SLNB) is the preferred technique.

Breast Reconstruction

Discuss immediate breast reconstruction with all patients who are being advised to have a mastectomy, and offer it except where significant comorbidity or (the need for) adjuvant therapy may preclude this option. All appropriate breast reconstruction options should be offered and discussed with patients, irrespective of whether they are all available locally.

Adjuvant Therapy Planning

- Start adjuvant chemotherapy or radiotherapy as soon as clinically possible within 31 days of completion of surgery* in patients with early breast cancer having these treatments.

Aromatase Inhibitors

- Postmenopausal women with oestrogen receptor (ER)-positive early invasive breast cancer who are not considered to be at low risk ** should be offered an aromatase inhibitor, either anastrozole or letrozole, as their initial adjuvant therapy. Offer tamoxifen if an aromatase inhibitor is not tolerated or contraindicated.

Assessment of Bone Loss

- Patients with early invasive breast cancer should have a baseline dual energy X-ray absorptiometry (DEXA) scan to assess bone mineral density if they:
    - Are starting adjuvant aromatase inhibitor treatment
    - Have treatment-induced menopause
    - Are starting ovarian ablation/suppression therapy

Primary Systemic Therapy

- Treat patients with early invasive breast cancer, irrespective of age, with surgery and appropriate systemic therapy, rather than endocrine therapy alone, unless significant comorbidity precludes surgery.

Follow-Up Imaging

- Offer annual mammography to all patients with early breast cancer, including ductal carcinoma in situ (DCIS), until they enter the NHS Breast Screening Programme/Breast Test Wales Screening Programme. Patients diagnosed with early breast cancer who are already eligible for screening should have annual mammography for 5 years.

*Department of Health (2007) Cancer reform strategy. London: Department of Health. (At present no equivalent target has been set by the Welsh Assembly Government.)

**Low-risk patients are those in the EPG or GPG (excellent prognostic group or good prognostic group) in the Nottingham Prognostic Index (NPI), who have 10-year predictive survivals of 96% and 93%, respectively. They would have a similar prediction using Adjuvant! Online.

Clinical Follow-up

- Patients treated for breast cancer should have an agreed, written care plan, which should be recorded by a named healthcare professional (or professionals), a copy sent to the GP and a personal copy given to the patient. This plan should include: – designated named healthcare professionals
    - Dates for review of any adjuvant therapy
    - Details of surveillance mammography
    - Signs and symptoms to look for and seek advice on
    - Contact details for immediate referral to specialist care
    - Contact details for support services, for example support for patients with lymphoedema

IMPLEMENTATION TOOLS

Audit Criteria/Indicators
Clinical Algorithm
Patient Resources
Quick Reference Guides/Physician Guides
Resources
Slide Presentation

For information about availability, see the "Availability of Companion Documents" and "Patient Resources" fields below.

INSTITUTE OF MEDICINE (IOM) NATIONAL HEALTHCARE QUALITY REPORT CATEGORIES

IOM CARE NEED

Getting Better
Living with Illness

IOM DOMAIN

Effectiveness
Patient-centeredness

IDENTIFYING INFORMATION AND AVAILABILITY

BIBLIOGRAPHIC SOURCE(S)

National Collaborating Centre for Cancer. Early and locally advanced breast cancer: diagnosis and treatment. London (UK): National Institute for Health and Clinical Excellence (NICE); 2009 Feb. 37 p. (NICE clinical guideline; no. 80).

ADAPTATION

Not applicable: The guideline was not adapted from another source.

DATE RELEASED

2006 Aug (revised 2009 Feb)

GUIDELINE DEVELOPER(S)

National Collaborating Centre for Cancer - National Government Agency [Non-U.S.]

SOURCE(S) OF FUNDING

National Institute for Health and Clinical Excellence (NICE)

GUIDELINE COMMITTEE

Guideline Development Group

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FINANCIAL DISCLOSURES/CONFLICTS OF INTEREST

At the start of the guideline development process all Guideline Development Group (GDG) members' interests were recorded on a standard declaration form that covered consultancies, fee-paid work, share-holdings, fellowships and support from the healthcare industry. At all subsequent GDG meetings, members declared new, arising conflicts of interest which were always recorded (see Appendix 8.1 of the full version of the original guideline document).

GUIDELINE STATUS

This is the current release of the guideline.

This guideline updates previous versions: National Institute for Health and Clinical Excellence (NICE). Trastuzumab for the adjuvant treatment of early-stage HER2-positive breast cancer. London (UK): National Institute for Health and Clinical Excellence (NICE); 2006 Aug. 23 p. (Technology appraisal guidance; no. 107).

National Institute for Health and Clinical Excellence (NICE). Paclitaxel for the adjuvant treatment of early node-positive breast cancer. London (UK): National Institute for Health and Clinical Excellence (NICE); 2006 Sep. 18 p. (Technology appraisal guidance; no. 108).

National Institute for Health and Clinical Excellence (NICE). Docetaxel for the adjuvant treatment of early node-positive breast cancer. London (UK): National Institute for Health and Clinical Excellence (NICE); 2006 Sep. 21 p. (Technology appraisal guidance; no. 109).

GUIDELINE AVAILABILITY

Electronic copies: Available in Portable Document Format (PDF) format from the National Institute for Health and Clinical Excellence (NICE) Web site.

AVAILABILITY OF COMPANION DOCUMENTS

The following are available:

- Early and locally advanced breast cancer: diagnosis and treatment. Full guideline. London (UK): National Institute for Health and Clinical Excellence (NICE); 2009 Feb. 167 p. (Clinical guideline; no. 80). Electronic copies: Available in Portable Document Format (PDF) format from the National Institute for Health and Clinical Excellence (NICE) Web site.

- Early and locally advanced breast cancer. Diagnosis and treatment. Quick reference guide. London (UK): National Institute for Health and Clinical Excellence; 2009 Feb. 20 p. (Clinical guideline; no. 80). Electronic copies: Available in Portable Document Format (PDF) from the NICE Web site.
- Early and locally advanced breast cancer. Diagnosis and treatment. Audit support. London (UK): National Institute for Health and Clinical Excellence; 2009, 12 p. (Clinical guideline; no. 80). Electronic copies: Available in Portable Document Format (PDF) from the NICE Web site.
- Early and locally advanced breast cancer. Diagnosis and treatment. Costing report. Implementing NICE guidance. London (UK): National Institute for Health and Clinical Excellence; 2009 Feb. 33 p. (Clinical guideline; no. 80). Electronic copies: Available in Portable Document Format (PDF) from the NICE Web site.
- Early and locally advanced breast cancer. Diagnosis and treatment. Costing template. London (UK): National Institute for Health and Clinical Excellence; 2009 Feb. Various p. (Clinical guideline; no. 80). Electronic copies: Available in Portable Document Format (PDF) from the NICE Web site.
- Early and locally advanced breast cancer. Implementing NICE guidance. Slide set. London (UK): National Institute for Health and Clinical Excellence; 2009. 22 p. (Clinical guideline; no. 80). Electronic copies: Available in Portable Document Format (PDF) from the NICE Web site.
- The guidelines manual 2007. London (UK): National Institute for Health and Clinical Excellence (NICE); 2007 April. Electronic copies: Available in Portable Document Format (PDF) from the NICE Web site.

Print copies: Available from the National Health Service (NHS) Response Line 0870 1555 455. ref: N1792. 11 Strand, London, WC2N 5HR.

PATIENT RESOURCES

The following is available:

- Early and locally advanced breast cancer. Understanding NICE guidance - Information for people who use NHS services. London (UK): National Institute for Health and Clinical Excellence; 2009 Feb. 20 p. (Clinical guideline; no. 80). Electronic copies: Available in Portable Document Format (PDF) from the National Institute for Health and Clinical Excellence (NICE) Web site.

Print copies: Available from the National Health Service (NHS) Response Line 0870 1555 455. ref: N1793. 11 Strand, London, WC2N 5HR.

NGC STATUS

This NGC summary was completed by ECRI Institute on August 1, 2007. This NGC summary was updated by ECRI Institute on August 25, 2009.

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